

Department of Health and Human Services

Part 1. Overview Information

Participating Organization(s) National Institutes of Health (NIH (http://www.nih.gov))
Components of Participating Organizations Office of Strategic Coordination (Common Fund (https://commonfund.nih.gov/)) This Notice of Funding (NOFO) is developed as a Common Fund initiative (https://commonfund.nih.gov/ (https://commonfund.nih.gov/)) through the Office of the NIH Director, Office of Strategic Coordination (https://commonfund.nih.gov/ (https://commonfund.nih.gov/)). All NIH Institutes and Centers participate in Common Fund initiatives. The NOFO will be administered by the National Institute of Mental Health (https://www.nimh.nih.gov/) on behalf of the NIH.
 Note: Not all NIH Institutes, Centers, and Offices (ICOs) participate in Announcements. Applicants should carefully note which ICOs participate in this announcement and view their respective areas of research interest at the ICO-Specific Scientific Interests website (https://grants.nih.gov/funding/find-a-fit-for-your-research/nih-institutes-centers-offices) . ICOs that do not participate in this announcement will not consider applications for funding.
Funding Opportunity Title Model-to-Clinic (M2C) for Precision Medicine with AI: Integrating Imaging with Multimodal Data (PRIMED-AI) (UG3/UH3, Clinical Trial Optional)
Activity Code UG3 (http://grants.nih.gov/grants/funding/ac_search_results.htm?text_curr=ug3&Search.x=0&Search.y=0&Search_Type=Activity) / UH3 (http://grants.nih.gov/grants/funding/ac_search_results.htm?text_curr=uh3&Search.x=0&Search.y=0&Search_Type=Activity) Exploratory/Developmental Phased Award Cooperative Agreement
Announcement Type New
Related Notices Check for any recent Notices of NIH Policy Changes (https://grants.nih.gov/grants/guide/url_redirect.php?id=11163) that may impact application requirements.
Funding Opportunity Number (FON) RFA-RM-27-013
Companion Funding Opportunity RFA-RM-27-011 (https://www.grants.gov/search-results-detail/359271) , U01 (https://grants.nih.gov/grants/funding/ac_search_results.htm?text_curr=U01&&Search.x=0&&Search.y=0&&Search_Type=Activity) Research Project (Cooperative Agreements) RFA-RM-27-012 (https://www.grants.gov/search-results-detail/359270) , UG3 (https://grants.nih.gov/grants/funding/ac_search_results.htm?text_curr=UG3&&Search.x=0&&Search.y=0&&Search_Type=Activity) / UH3 (https://grants.nih.gov/grants/funding/ac_search_results.htm?text_curr=UH3&&Search.x=0&&Search.y=0&&Search_Type=Activity) Phase 1 Exploratory/Developmental Cooperative Agreement/Exploratory/Developmental Cooperative Agreement Phase II RFA-RM-27-014 (https://www.grants.gov/search-results-detail/359269) , U54 (https://grants.nih.gov/grants/funding/ac_search_results.htm?text_curr=U54&&Search.x=0&&Search.y=0&&Search_Type=Activity) Specialized Center (Cooperative Agreements) RFA-RM-27-015 (https://www.grants.gov/search-results-detail/359268) , U24 (https://grants.nih.gov/grants/funding/ac_search_results.htm?text_curr=U24&&Search.x=0&&Search.y=0&&Search_Type=Activity) Resource-Related Research Project (Cooperative Agreements)
Number of Applications See Part 2, Section III. 3. Additional Information on Eligibility.
Assistance Listing Number(s) 93.310
Funding Opportunity Purpose The overarching goal of this notice of funding opportunity (NOFO) and its companion opportunities is to establish the Precision Medicine with AI: Integrating Imaging with Multimodal Data (PRIMED-AI) Program to support development of innovative, reliable, cost-effective, and sustainable multimodal AI-based clinical decision support (CDS) tools. PRIMED-AI CDS tools are based on the integration of clinical imaging with other types of multimodal health data to enhance care for patients with a wide range of health conditions.

The PRIMED-AI Program seeks to catalyze the adoption of AI-based CDS tools into clinical workflows to enable novel personalized medicine strategies that address significant health challenges.

The purpose of this NOFO is to catalyze the translation of Artificial Intelligence (AI)-enabled, image-centered, multimodal CDS tools, developed as Software as a Medical Device, from training and testing of prototypes towards clinical applications that address unmet health challenges in precision medicine. These projects are expected to have high potential for demonstrable, positive impact on patient outcomes and/or healthcare processes.

Funding Opportunity Goal(s)

The Office of Strategic Coordination ([Common Fund \(https://commonfund.nih.gov/\)](https://commonfund.nih.gov/)) supports research and other projects that will accelerate fundamental biomedical discovery and translation of that knowledge into effective prevention strategies and new treatments.

Key Dates

Posted Date

June 30, 2026

Open Date (Earliest Submission Date)

September 19, 2026

Application Due Dates			Review and Award Cycles		
New	Renewal / Resubmission / Revision (as allowed)	AIDS - New/Renewal/Resubmission/Revision, as allowed	Scientific Merit Review	Advisory Council Review	Earliest Start Date
October 19, 2026	Not Applicable	Not Applicable	March 2027	May 2027	July 2027

All applications are due by 5:00 PM local time of applicant organization.

Applicants are encouraged to apply early to allow adequate time to make any corrections to errors found in the application during the submission process by the due date.

No late applications will be accepted for this Notice of Funding Opportunity (NOFO).

Due Dates for E.O. 12372

Not Applicable

Expiration Date

October 20, 2026

Required Application Instructions

It is critical that applicants follow the instructions in the Research (R) Instructions in the [How to Apply - Application Guide \(https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400\)](https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400), except where instructed to do otherwise (in this NOFO or in a Notice from [NIH Guide for Grants and Contracts \(http://grants.nih.gov/grants/guide/url_redirect.htm?id=11164\)](http://grants.nih.gov/grants/guide/url_redirect.htm?id=11164)).

Conformance to all requirements (both in the Application Guide and the NOFO) is required and strictly enforced. Applicants must read and follow all application instructions in the Application Guide as well as any program-specific instructions noted in Section IV. When the program-specific instructions deviate from those in the Application Guide, follow the program-specific instructions.

Applications that do not comply with these instructions may be delayed or not accepted for review.

There are several options available to submit your application through Grants.gov to NIH and Department of Health and Human Services partners. You **must** use one of these submission options to access the application forms for this opportunity.

1. Use the [NIH ASSIST system \(https://public.era.nih.gov/assist/public/login.era\)](https://public.era.nih.gov/assist/public/login.era) to prepare, submit and track your application online.
2. Use an institutional system-to-system (S2S) solution to prepare and submit your application to Grants.gov and [eRA Commons \(https://public.era.nih.gov/commons/\)](https://public.era.nih.gov/commons/) to track your application. Check with your institutional officials regarding availability.
3. Use [Grants.gov \(https://grants.gov/search-grants?oppStatuses=closed|archived|posted|forecasted&fon=PA-25-301\)](https://grants.gov/search-grants?oppStatuses=closed|archived|posted|forecasted&fon=PA-25-301) Workspace to prepare and submit your application and [eRA Commons \(http://public.era.nih.gov/commons/\)](http://public.era.nih.gov/commons/) to track your application.

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Part 2. Full Text of Announcement

Section I. Notice of Funding Opportunity Description

Purpose

The Precision Medicine with AI: Integrating Imaging with Multimodal Data (PRIMED-AI) NOFOs seek to spur on the development of innovative, reliable, cost-effective, and sustainable multimodal AI-based clinical decision support (CDS) tools with the potential for transformational impact. Overall, the PRIMED-AI Program catalyzes the integration of clinical imaging with other types of multimodal health data that informs CDS tool development and testing in clinical workflows, which serves to enhance patient care for a wide range of health conditions.

The Model-to-Clinic (M2C) NOFO uniquely seeks projects that take CDS tools developed as Software as a Medical Device (SaMD), from validated prototypes to clinical applications.

M2C projects are structured as phased innovation awards (UG3/UH3) designed to advance multimodal AI-based CDS tools through progressive stages of development and validation.

UG3 Phase (Exploratory/Developmental): This initial phase focuses on establishing the technical and operational foundation for clinical translation. Projects will develop and refine AI models, regulatory preparations, clinical implementation infrastructure, deployment strategies, and demonstrate preliminary feasibility in target clinical settings. Milestones must be achieved before transitioning to the UH3 phase.

UH3 Phase (Advanced Development): Following successful completion of the UG3 phase, the UH3 phase emphasizes CDS model clinical implementation and validation. Projects will deploy CDS tools in clinical workflows; conduct prospective clinical studies to evaluate performance; demonstrate potential for impact and integration with existing health IT systems; and generate evidence for broader adoption and sustainability. Projects must demonstrate measurable potential for clinical impact and pathway(s) to sustained use beyond the award period.

The combined UG3/UH3 award period cannot exceed 5 years total. Transition from UG3 to UH3 requires achieving specified milestones and NIH approval.

M2C projects are expected to have high potential for demonstrable, positive impact on patient outcomes and/or healthcare processes.

Key Terms used in PRIMED-AI Program

- Clinical decision support (CDS) tool.** A type of software, computational model or digital system that is incorporated into clinical workflows to assist in determining a course of action related to patient care.
- Clinical imaging.** Any FDA-approved imaging modality used in patient care, including radiologic (e.g., radiographic, computed tomographic, magnetic resonance, molecular, radionuclide imaging), ophthalmologic (e.g., Optical Coherence Tomography), endoscopic, and dermatologic imaging, and video. Clinical imaging of human participants is intended to be the anchor data type that multimodal data are integrated with in the PRIMED-AI Program, which will form the basis for AI algorithm development and testing of CDS tools.
- DICOM standard.** Digital Imaging and Communications in Medicine (DICOM) standard, the most widely used by the community to address interoperability challenge, is strongly encouraged but not required. Inclusion of non-DICOM standard clinical imaging must include a plan to develop standards in conjunction with the PRIMED-AI community if none currently exist.
- Harmonization.** The process of bringing together data from different sources and ensuring that it is consistent, comparable, and compatible. This involves standardizing data formats, structures, and definitions so that data from various sources can be integrated and analyzed together effectively.
- Interoperability.** The ability for AI models and associated data and metadata to be understood and work across different AI platforms and have the potential to be used consistently across different health systems.
- Multimodal data (MMD).** Representing different types of data and information from multiple sources that may include multiple clinical imaging modalities and non-imaging health data (e.g., electronic health records, EEG, EKG, laboratory test results (-omics), wearable sensor data, medical reports). Multiscale data are encouraged; however, microscopy-based imaging of biospecimens *ex vivo* (e.g., digital pathology) cannot represent the sole imaging data type. Although non-human imaging and/or MMD data may have assisted in development of an AI-model, overt representation and reliance on data derived from non-human sources for CDS tool development, testing, and validation will be given low programmatic priority.
- Playbook.** A collection of actionable guidelines, standardized protocols, and/or standardized operating procedures for the reliable and effective development and deployment of multimodal clinical decision support tools. The Playbook is a collection of frameworks.
- Precision Medicine.** Sometimes called personalized medicine or individualized medicine, refers to a healthcare approach that uses information based on a patient's individual characteristics such as health measures, genotype, phenotype, environment, and lifestyle information to guide, tailor, and optimize decisions related to their medical care and management.
- PRIMED-AI Consortium.** The consortium constitutes members of PRIMED-AI excluding NIH program staff. PRIMED-AI Program is an umbrella term encompassing the consortium, NIH staff, and overall programmatic objectives.
- Uncertainty Quantification.** Measuring or quantifying the impact of uncertainties in complex systems, including quantifying the confidence in outcomes predicted by multimodal AI models.
- Validation.** Validation exists on a continuum in the PRIMED-AI Program. Analytical or technical validation is based on the evaluation of algorithmic performance and the ability of a multimodal AI model to make accurate predictions. Initially, a model or algorithm can meet expected performance on retrospective and/or entirely new clinical datasets within the confines of a specific hospital or healthcare system. It is useful locally (internally) but is not yet applicable (generalizable) to the wider real-world population. Subsequently, for clinical validation, a model or algorithm can be tested (externally) on new wider real-world population datasets to predict a meaningful outcome and meet regulatory criteria for the claimed use case. The PRIMED-AI Program anticipates validation of projects along this continuum as outlined in the NOFOs.
- Verification.** The process by which data integrity and construction of models is assessed for appropriateness within the context of use or intended purpose.

Background

Clinical imaging plays a pivotal role in diagnosis, treatment, and assessment of health outcomes; however, it is often utilized in isolation from other types of data during the development of artificial intelligence (AI)-based clinical decision support (CDS) tools. Current AI applications typically leverage a single imaging modality from radiological or ophthalmological sources. Because health is shaped by a variety of interconnected factors—clinical, biological, genetic, environmental and social—the **Precision Medicine with AI: Integrating Imaging with Multimodal Data (PRIMED-AI) Program** seeks to integrate clinical imaging with relevant, complementary multimodal data (MMD). The overarching goal of the PRIMED-AI Program is to catalyze the development and adoption of innovative AI-based CDS tools into clinical workflows. The PRIMED-AI Program initiatives collectively aim to tackle complex clinical challenges by fostering cross-disciplinary collaboration to create innovative, reliable, cost-effective, and sustainable AI solutions that enable precision medicine strategies.

Prior to applying, applicants are encouraged to check the [PRIMED-AI Program website \(https://commonfund.nih.gov/primed-ai\)](https://commonfund.nih.gov/primed-ai) for updates to relevant FAQs and informational webinars, and are also encouraged to read all companion NOFOs to ensure they are aware of the goals and responsibilities of all PRIMED-AI award recipients, including methods PRIMED-AI intends to utilize to address error mitigation and technical management. Familiarity with the companion NOFOs may better inform proposed M2C interconnections with other aspects of the PRIMED-AI Program.

M2C CDS tools aim to enhance diagnostic accuracy, optimize treatment, improve prognostic prediction, and streamline workflows for clinical decision-making through processing and integration of complex, multimodal data streams to ultimately improve patient outcomes and/or lower patient care costs. This initiative and its companion Data-to-Model Academic-Industrial Partnership (D2M-AIP) directly address a critical translational gap in AI research—the gap between promising AI prototypes developed in controlled research environments and

robustly validated, clinically deployable CDS tools that function reliably in real-world healthcare settings. For the purpose of these NOFOs, applicants must demonstrate sufficient access to verified, comprehensive, and complex multimodal datasets as well as integration and harmonization of these data to address a target clinical application. Applicants to the *M2C* must have a technically validated AI prototype, defined as a model that has undergone technical validation at a minimum of a single site, or unimodally, or in retrospective data, or distinctly validated model types that need to be integrated (e.g., hybrid models that combine different types of data or logic such as machine learning-based with rule-based, or logic-based, neuromorphic based, or dynamical system theories).

During the PRIMED-AI project period, *M2C* projects must perform comprehensive technical and clinical validation, beyond single-site studies to ensure broad clinical applicability. Ultimately, the *M2C* NOFO aims to deliver a set of valuable and effective CDS tools able to perform appropriately in real-world clinical settings within a precision medicine framework.

The value of any CDS tool developed under this program is contingent upon its relevance, reliability, and broad clinical adoption to improve patient care and reduce patient care costs.

Distinction Between Model-to-Clinic (*M2C*) and Data-to-Model Academic Industrial Partnerships (*D2M-AIP*) NOFOs

The PRIMED-AI Program includes two parallel NOFOs designed with distinct primary foci along the data-to-model-to-clinic continuum. *To help applicants select the appropriate funding opportunity, the essential differences are summarized here:*

- ***M2C*** projects primarily focus on assessing clinical adoption and impact by translating a promising AI model(s) into a clinical workflow as CDS tools. *M2C* projects must conduct clinical validation studies to evaluate real-world utility for adoption in clinical care. *M2C* projects begin with a promising AI model and aim to assess and validate its clinical performance, utility, and impact in real-world healthcare settings. They should also address challenges related to adopting AI-assisted CDS tools in clinical workflows, including associated costs and feasibility.
- ***D2M-AIP*** projects aim towards commercialization and are led by an academic-industrial partnership that primarily focuses on novel data integration and/or new AI model development. Projects proposed under *D2M-AIP* exist in the pre-competitive space and will emphasize technical validation and performance testing, without requiring clinical validation studies within the award period. The goal is to develop and de-risk novel AI technologies through collaboration, preparing them for future commercialization, adoption, and use of a CDS tool(s).

Key Requirements

M2C projects supported by this NOFO will involve two distinct, milestone-driven phases of innovation research and development. In the UG3 phase, *M2C* award recipients will make the CDS tools deployable and generalizable across multiple sites, integrating comprehensive, large-scale, clinical imaging and multimodal datasets. In the UH3 phase, applicants apply these tools in the clinical setting with the potential for transformative impact on real-world challenges in precision medicine. Applications must be built upon the following five pillars (further specified in Section IV):

1. Data Quality and Governance for Model Development
2. Clinically Grounded AI Technology
3. Pathway to Implementation and Adoption
4. Integrated Multidisciplinary Team
5. Error Mitigation and Technical Management

Applications Not Responsive to this NOFO.

To be considered responsive, applications must align with the central goal of the PRIMED-AI Program.

The following types of applications will be considered non-responsive and will not be reviewed:

- Projects primarily focused on basic research in AI/ML methodology without a clear and significant translational goal towards a specific clinical problem.
- Projects that do not focus on the translation of a CDS tool that uses clinical imaging as the anchor data type, integrated with other multimodal data. Clinical imaging must be the modality that anchors the model. Digital pathology cannot represent the imaging anchor data type but may serve as a form of multimodal data. Projects where the primary focus is on a mechanistic biological research question and the AI technology and methods are already well-established, adapted, optimized, and validated for that context of use.
- Applications proposing Phase III clinical trials as the primary scope of work. (Note: While this NOFO is "Clinical Trial Optional," large-scale, confirmatory Phase III trials are outside the scope).
- Projects that do not define a targeted unmet clinical problem (intended use) on a clinical population (intended users) for the proposed CDS tool.
- Projects without an existing prototype of an AI-powered, image-centered, multimodal CDS tool.

Investigators proposing NIH-defined clinical trials may refer to the [Research Methods Resources \(https://researchmethodsresources.nih.gov/\)](https://researchmethodsresources.nih.gov/) website for information about developing statistical methods and study designs.

See Section VIII. Other Information for award authorities and regulations.

Section II. Award Information

Funding Instrument

Cooperative Agreement: A financial assistance mechanism used when there will be substantial Federal scientific or programmatic involvement. Substantial involvement means that, after award, NIH scientific or program staff will assist, guide, coordinate, or participate in project activities. See Section VI.2 for additional information about the substantial involvement for this NOFO.

Application Types Allowed

New

The [OER Glossary \(http://grants.nih.gov/grants/guide/uri_redirect.htm?id=11116\)](http://grants.nih.gov/grants/guide/uri_redirect.htm?id=11116) and the How to Apply Application Guide provide details on these application types. Only those application types listed here are allowed for this NOFO.

Clinical Trial?

Optional: Accepting applications that either propose or do not propose clinical trial(s).

[Need help determining whether you are doing a clinical trial? \(https://grants.nih.gov/grants/guide/uri_redirect.htm?id=82370\)](https://grants.nih.gov/grants/guide/uri_redirect.htm?id=82370)

Funds Available and Anticipated Number of Awards

The NIH Common Fund intends to commit funds for approximately 6-8 UG3/UH3 awards. The number of awards is contingent upon NIH appropriations and the submission of a sufficient number of meritorious applications.

Award Budget

Applicants should request a budget appropriate for the proposed scope of work, not to exceed \$450,000 in direct costs per year for UG3 and \$1,000,000 in direct costs for UH3 phases.

Award Project Period

The total project period for a UG3/UH3 award may not exceed 5 years.

NIH grants policies as described in the [NIH Grants Policy Statement \(http://grants.nih.gov/grants/guide/url_redirect.htm?id=11120\)](http://grants.nih.gov/grants/guide/url_redirect.htm?id=11120) will apply to the applications submitted and awards made from this NOFO.

Section III. Eligibility Information

1. Eligible Applicants

Eligible Organizations

Higher Education Institutions - Includes all types

- Public/State Controlled Institutions of Higher Education
- Private Institutions of Higher Education

Nonprofits Other Than Institutions of Higher Education

- Nonprofits with 501(c)(3) IRS Status (Other than Institutions of Higher Education)
- Nonprofits without 501(c)(3) IRS Status (Other than Institutions of Higher Education)

For-Profit Organizations

- Small Businesses
- For-Profit Organizations (Other than Small Businesses)

Local Governments

- State Governments
- County Governments
- City or Township Governments
- Special District Governments
- Indian/Native American Tribal Governments (Federally Recognized)
- Indian/Native American Tribal Governments (Other than Federally Recognized).

Federal Governments

- U.S. Federal Government Agencies (e.g., NIH Intramural Research Program, DOE National Laboratories) may participate as partners but are not eligible to apply as the primary applicant institution
- U.S. Territory or Possession

Other

- Independent School Districts
- Public Housing Authorities/Indian Housing Authorities
- Native American Tribal Organizations (other than Federally recognized tribal governments)
- Faith-based or Community-based Organizations
- Regional Organizations
- Non-domestic (non-U.S.) Entities (Foreign Organizations)

Foreign Organizations/International Collaborations

Non-domestic (non-U.S.) Entities (Foreign Organizations) **are** eligible to apply.

Non-domestic (non-U.S.) components of U.S. Organizations **are** eligible to apply.

Foreign components, as [defined in the NIH Grants Policy Statement \(http://grants.nih.gov/grants/guide/url_redirect.htm?id=11118\)](http://grants.nih.gov/grants/guide/url_redirect.htm?id=11118), **are** allowed.

NIH will no longer issue awards (i.e., new, renewal, or non-competing continuation) to domestic or foreign entities that involve foreign subawards/subcontracts. All NIH-funded research involving foreign subawards/subcontracts must be submitted in response to a NOFO that is specifically designated for funded international collaborations. See [NIH Grants Policy Statement 16.8 Collaborative International Research Awards \(https://grants.nih.gov/grants/policy/nihgps/HTML5/section_16/16.8_collab_int_res_awards.htm\)](https://grants.nih.gov/grants/policy/nihgps/HTML5/section_16/16.8_collab_int_res_awards.htm).

Applications involving foreign subawards/subcontracts submitted in response to this NOFO will be deemed noncompliant and will not be considered for funding. This policy applies to all monetary international collaborations resulting in foreign subawards/subcontracts, however, it does not preclude unfunded international collaborations or [foreign components \(https://grants.nih.gov/grants/policy/nihgps/HTML5/section_1/1.2_definition_of_terms.htm\)](https://grants.nih.gov/grants/policy/nihgps/HTML5/section_1/1.2_definition_of_terms.htm), funding for foreign consultants, or procurement of unique equipment or supplies from foreign vendors.

Required Registrations

Applicant Organizations

Applicant organizations must complete and maintain the following registrations as described in the How to Apply- Application Guide to be eligible to apply for or receive an award. All registrations must be completed prior to the application being submitted. Registration can take 6 weeks or more, so applicants should begin the registration process as soon as possible. Failure to complete registrations in advance of a due date is not a valid reason for a late submission, please reference the [NIH Grants Policy Statement Section 2.3.9.2 Electronically Submitted Applications \(http://grants.nih.gov/grants/guide/url_redirect.htm?id=82423\)](http://grants.nih.gov/grants/guide/url_redirect.htm?id=82423) for additional information.

- **System for Award Management (SAM)** (https://grants.nih.gov/grants/guide/url_redirect.htm?id=82390) – Applicants must complete and maintain an active registration, **which requires renewal at least annually**. The renewal process may require as much time as the initial registration. SAM registration includes the assignment of a Commercial and Government Entity (CAGE) Code for domestic organizations which have not already been assigned a CAGE Code. Foreign organizations must obtain a **NATO Commercial and Government Entity (NCAGE) Code** (http://grants.nih.gov/grants/guide/url_redirect.htm?id=11176) (in lieu of a CAGE code) in order to register in SAM.
 - Unique Entity Identifier (UEI)– A UEI is issued as part of the SAM.gov registration process. The same UEI must be used for all registrations, as well as on the grant application.
- **eRA Commons** (https://grants.nih.gov/grants/guide/url_redirect.htm?id=11123) - Once the unique organization identifier is established, organizations can register with eRA Commons in tandem with completing their Grants.gov registrations; all registrations must be in place by time of submission. eRA Commons requires organizations to identify at least one Signing Official (SO) and at least one Program Director/Principal Investigator (PD/PI) account in order to submit an application.
- **Grants.gov** (http://grants.nih.gov/grants/guide/url_redirect.htm?id=82300) – Applicants must have an active SAM registration in order to complete the Grants.gov registration.

Program Directors/Principal Investigators (PD(s)/PI(s))

All PD(s)/PI(s) must have an eRA Commons account. PD(s)/PI(s) should work with their organizational officials to either create a new account or to affiliate their existing account with the applicant organization in eRA Commons. If the PD/PI is also the organizational Signing Official, they must have two distinct eRA Commons accounts, one for each role. Obtaining an eRA Commons account can take up to 2 weeks.

All PD(s)/PI(s) must be registered with **ORCID** (<https://orcid.org/>). The personal profile associated with the PD(s)/PI(s) eRA Commons account must be linked to a valid ORCID ID. For more information on linking an ORCID ID to an eRA Commons personal profile see the **ORCID topic in our eRA Commons online help** (<https://era.nih.gov/erahelp/Commons/default.htm#orcid.htm%3FTocPath%3D29>).

Eligible Individuals (Program Director/Principal Investigator)

Any individual(s) with the skills, knowledge, and resources necessary to carry out the proposed research as the Program Director(s)/Principal Investigator(s) (PD(s)/PI(s)) is invited to work with their organization to develop an application for support.

For institutions/organizations proposing multiple PDs/PIs, visit the Multiple Program Director/Principal Investigator Policy and submission details in the Senior/Key Person Profile (Expanded) Component of the How to Apply–Application Guide.

Investigators from U.S. Federal Government Agencies (see eligibility statement above) may participate in this program as unpaid collaborators, co-Is, or unpaid consultants in accord with the Terms and Conditions provided in this NOFO. While their expertise and resources are highly valued, NIH intramural scientists cannot receive salary support or any other direct financial compensation from funds awarded through this extramural NOFO. Their involvement should be clearly outlined in the application, including a description of their scientific contribution, their number of person-months devoted to the project, and a formal letter of collaboration from their Institute/Center Scientific Director or equivalent, confirming their commitment to the project and that no grant funds will be used for their support or the operational costs of NIH intramural facilities. Any use of NIH intramural resources should be fully justified and approved by the relevant NIH Institute/Center. The grant applicant is responsible for writing the section of the grant that describes the proposed collaboration within the grant, which the NIH investigator should see and approve. Intellectual property will be managed in accord with established policy of the NIH in compliance with Executive Order 10096, as amended, 45 CFR Part 7; patent rights for inventions developed in NIH facilities are NIH property unless NIH waives its rights.

Specific Eligibility for Federally Funded Research and Development Centers (FFRDCs) and University Affiliated Research Centers (UARCs): FFRDCs and UARCs may not apply to this Research Opportunity Announcement as a prime performer/lead institution; however, subject to any restrictions (i.e., direct competition limitations as determined by the entity or potential limiting organizational conflicts of interest, agency sponsor related requirements and policies, etc.), FFRDCs and UARCs may be included as part the prime performer's proposal, as a sub-awardee. As with all prime/sub-awardee teaming arrangements, the Government will only have privity of contract with the prime performer, and all payments will be made through the prime awardee.

Foreign applicants

- Will require strong justification
- U.S. collaborators encouraged
- Subawards for foreign investigators **are not** allowed
- Unpaid foreign collaborators **are** allowed

2. Cost Sharing

This NOFO does not require cost sharing as defined in the **NIH Grants Policy Statement Section 1.2 Definition of Terms** (http://grants.nih.gov/grants/guide/url_redirect.htm?id=11126).

3. Additional Information on Eligibility

Number of Applications

Applicant organizations may submit more than one application, provided that each application is scientifically distinct.

The NIH will not accept duplicate or highly overlapping applications under review at the same time, per **NIH Grants Policy Statement Section 2.3.7.4 Submission of Resubmission Application** (http://grants.nih.gov/grants/guide/url_redirect.htm?id=82415). This means that the NIH will not accept:

- A new (A0) application that is submitted before issuance of the summary statement from the review of an overlapping new (A0) or resubmission (A1) application.
- A resubmission (A1) application that is submitted before issuance of the summary statement from the review of the previous new (A0) application.
- An application that has substantial overlap with another application pending appeal of initial peer review (see **NIH Grants Policy Statement 2.3.9.4 Similar, Essentially Identical, or Identical Applications** (http://grants.nih.gov/grants/guide/url_redirect.htm?id=82423)).

Section IV. Application and Submission Information

1. Requesting an Application Package

The application forms package specific to this opportunity must be accessed through ASSIST, Grants.gov Workspace or an institutional system-to-system solution. Links to apply using ASSIST or Grants.gov Workspace are available in Part 1 of this NOFO. See your administrative office for instructions if you plan to use an institutional system-to-system solution.

2. Content and Form of Application Submission

It is critical that applicants follow the instructions in the Research (R) Instructions in the **How to Apply - Application Guide** (https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400) except where instructed in this notice of funding opportunity to do otherwise (in this NOFO, in a **policy notice** (https://grants.nih.gov/grants/guide/url_redirect.php?id=11163), or other notice from **NIH Guide for Grants and Contracts** (https://grants.nih.gov/grants/guide/url_redirect.php?id=11164)). Conformance to the requirements in the Application Guide is required and strictly enforced. Applications that are out of compliance with these instructions may be delayed or not accepted for review.

Page Limitations

All page limitations described in the **How to Apply- Application Guide** (<https://grants.nih.gov/grants/how-to-apply-application-guide.html>) and the **Table of Page Limits** (https://grants.nih.gov/grants/guide/url_redirect.htm?id=61134) must be followed.

Instructions for Application Submission

The following section supplements the instructions found in the [How to Apply- Application Guide \(https://grants.nih.gov/grants/how-to-apply-application-guide.html\)](https://grants.nih.gov/grants/how-to-apply-application-guide.html) and should be used for preparing an application to this NOFO.

SF424(R&R) Cover

All instructions in the [How to Apply - Application Guide \(https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400\)](https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400) must be followed.

SF424(R&R) Project/Performance Site Locations

All instructions in the [How to Apply- Application Guide \(https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400\)](https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400) must be followed.

SF424(R&R) Other Project Information

All instructions in the [How to Apply- Application Guide \(https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400\)](https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400) must be followed.

SF424(R&R) Senior/Key Person Profile

All instructions in the [How to Apply- Application Guide \(https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400\)](https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400) must be followed.

R&R Budget

All instructions in the [How to Apply- Application Guide \(https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400\)](https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400) must be followed.

The budget request for this NOFO must distinguish between extramural costs and the costs associated with NIH intramural investigator participation. Extramural costs are those associated with the extramural investigator and the applicant organization.

Consistent with Section III eligibility requirements, NIH intramural investigators participate as unpaid collaborators and cannot receive salary support or any other direct financial compensation from funds awarded through this NOFO. However, applicants should identify and budget for reasonable costs of materials, supplies, and services necessary for the intramural investigator to carry out their proposed work (excluding salary, personnel costs, and operational costs of NIH intramural facilities). All use of NIH intramural resources must be fully justified in the budget justification and approved by the relevant NIH Institute/Center as confirmed in the letter of collaboration required in Section III.

Cost of NIH Intramural work

Please note that the NIH Intramural Research program (IRP) costs and participation will not be included in the award paid to the grantee. However, cost of IRP reagents, consumables and data analysis (e.g. software licenses) should be submitted as a separate budget page in the application. IRP budgets may not include any salary and related fringe benefits for career, career conditional or other federal employees (civilian or uniformed service) with permanent appointments under existing position ceilings or any costs related to administrative or facilities support (equivalent to Facilities and Administrative costs). These costs may include salary for staff to be specifically hired under a temporary appointment for the project. The IRP budget may also include consultant costs, equipment, supplies, travel, and other items typically listed under other expenses. Funds can be requested for services by an external investigator or contractor as a subcontract/consortium including the applicable indirect (F&A)

Extramural Grantee Costs

Extramural costs may include such items as salary support for the extramural PD/PI and staff at the applicant organization, supplies, laboratory animals, data analysis, and other allowable costs for work performed at the (extramural) applicant organization, as well as travel costs for the extramural investigator(s).

- The PD/PI and up to two other key personnel with complementary expertise are required to attend an annual in person Consortium meeting in Bethesda, MD, as well as virtual Consortium-led tutorials and open innovation meetings, as appropriate. Funds to attend these in person meetings should be budgeted in the application.

R&R Subaward Budget

All instructions in the [How to Apply - Application Guide \(https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400\)](https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400) must be followed.

PHS 398 Cover Page Supplement

All instructions in the [How to Apply - Application Guide \(https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400\)](https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400) must be followed.

PHS 398 Research Plan

All instructions in the [How to Apply - Application Guide \(https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400\)](https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400) must be followed, with the following additional instructions:

Applications must be built upon five core pillars, with a robust strategy for each. The first four pillars should be detailed within the 12-page application limit, while Pillar 5 must be submitted as a separate, required attachment. The entire strategy should be tailored to the specific aims of the project.

1. Data Quality and Governance for Model Development

- **Access to Clinical-Grade Imaging and Multimodal Datasets:** Applicants must provide verifiable evidence of access to comprehensive, large-scale datasets essential for the project's entire lifecycle (development, technical validation, clinical validation). A 'Data Risk Assessment and Mitigation Plan' is required to address potential challenges in data access, quality, and sharing.
- **Data Fitness-for-Purpose Framework:** Rather than general data sharing, applicants must present a systematic approach to data curation, harmonization, and quality management that ensures data is fit for the intended purpose of AI model development and validation. This framework must detail protocols for ensuring data integrity, tracking provenance, and addressing challenges inherent to multimodal data to ensure the resulting model is robust and reliable.

2. Clinically Grounded AI Technology

- **AI-Powered, Image-Centered, Multimodal CDS Tool:** The central output must be a SaMD tool that integrates meso-to-macro scale clinical imaging with at least one other data modality (e.g., clinical lab tests, 'omics,' digital sensor data). The research plan must clearly articulate how clinical imaging will serve as the anchor data type for the project. The tool must address a clearly defined and significant unmet clinical need.
- **Robust AI Architecture:** The proposal must describe an advanced analytical framework (e.g., deep learning, federated learning) optimized for multimodal data fusion. The architecture must be appropriate for the specific clinical task and data types.
- **End-User Design and Clinical Integration Plan:** Applicants must provide a detailed plan for the proposed CDS tool's translation, deployment, and use within a clinical workflow. This plan should include:
 - A discussion of the clinical problem and the current standard of care.
 - A clear description of the expected user group(s) and their clinical environments.
 - A concrete plan for how the CDS tool will be integrated into the clinical workflow.

3. Pathway to Implementation and Adoption

- **Clinical Adoption and Dissemination Strategy:** Applicants should describe a compelling vision for the tool's clinical adoption and dissemination including proactive regulatory engagement.

- **Model Performance Monitoring System:** All projects must include a plan for a system to track model performance and reliability. This plan must describe a post-deployment monitoring pipeline ready for clinical settings.

4. Integrated Multidisciplinary Team

- **Collaborative Structure:** Applications may use a multiple PD/PI mechanism.
- **Core Multidisciplinary Expertise:** Applicants must establish an inter-disciplinary, multi-institutional research team with the combined expertise necessary to address the proposed translational challenge. The team may include any number of participants and organizations necessary to assemble a critical mass of expertise and know-how for effective execution. The level of participation may vary among participants, based on the translational goals of the project. The team must possess the necessary expertise for the project's scope. Required expertise should include:
 - Medical device/SaMD development
 - Data science (AI/multimodal data)
 - Relevant clinical domain knowledge
 - Regulatory science (either on the team or through consultation)
 - Implementing clinical workflows for healthcare systems
 - Additionally, NIH encourages proposed projects to include:
 - Appropriate expertise to address user acceptance and human-AI interaction dynamics, for projects focusing on adoption and integration challenges.
 - Patient representatives or advocates to ensure patient-centered design principles are incorporated.
- **Investigator(s) and Environment Leadership Plan:** All applications must include a comprehensive Leadership Plan. The arrangements for collaborations must allow administration of the joint effort as a single project. An organizational structure that clearly defines the partnership and relationships among the various components must be described in the Leadership Plan and illustrated in an organizational chart. This plan should also describe
 - Publication and Public Dissemination Policy: For publications and other public dissemination of information, policies to address the ordering and recognition of authors, and decisions about what material to publish, consistent with the interests of commercial partners (where applicable) should be presented.
 - Conflict resolution procedure: Including an escalation pathway for disagreements that cannot be resolved at the PI level must involve pre-agreed arbitration or mediation processes and must also detail joint governance structures, IP management agreements, and publication policies agreed upon by all partners.
- **Resource Allocation:** Under terms and procedures to be defined in the Leadership Plan, the team has the responsibility and authority to use funds in the most productive way to achieve the goals defined at the time that the award is made. To accomplish these tasks, the PD(s)/PI(s) can adjust funding among M2C participants to support new partners or to reduce support to existing partners as needed.

5. Error Mitigation and Technical Management (Required Attachment)

Applicants must submit a required [Error Mitigation and Technical Management Plan \(https://commonfund.nih.gov/primed-ai/error-mitigation\)](https://commonfund.nih.gov/primed-ai/error-mitigation) as a separate attachment up to three pages in length that addresses all components listed in the linked guidance. The filename "Error Mitigation and Technical Management Plan.pdf" should be used for this attachment. This file name will be reflected in the final image bookmarking for easy access to reviewers. The Error Mitigation and Technical Management Plan may be revised during the award period in accordance with Consortium policies and updated NIH guidance.

Key Components of Phased Innovation Projects

M2C projects are phased innovation awards consisting of linked awards (UG3/UH3) for each phase. Approach is divided into two distinct parts corresponding to the UG3 and UH3 phases. The total duration of the UG3 and UH3 phases cannot exceed 5 years. At the end of the Approach section for the UG3 and UH3 subsections, milestones and timelines should be provided under separate headings.

Phase 1 (UG3) - Rigorous AI Model Refinement and Technical Validation (Up to 2 Years)

The UG3 phase focuses on the robust development and technical validation of CDS tools, preparing them for subsequent clinical application. All applicants must meet the following core requirements:

- **Rigorous Multimodal Data Management:** Projects must incorporate the integration and analysis of diverse modalities and data sources, with clinical imaging as the anchoring modality. This necessitates rigorous data preparation procedures that address variability in data format, resolution, completeness, and quality across all sources.
- **Co-design:** Employ a rigorous design approach that incorporates perspectives from different stakeholders including clinicians, patients, and other end-users. This systematic process must consider deployment context that could potentially influence both implementation success and user adoption. Co-design activities are required to begin during Phase 1 and continue throughout Phase 2.
- **Strategic Risk Mitigation:** A clear identification of high-risk technical assumptions in the proposed AI methodology is required. The UG3 phase must incorporate specific, early milestones designed to stress-test and mitigate these assumptions using diverse, heterogeneous datasets representative of real-world clinical data. Proposals must detail quantifiable go/no-go criteria directly linked to the successful validation of these core technical assumptions, with a particular focus on factors impacting real-world applicability.
- **Proactive Regulatory Engagement:** Active engagement with the Office of the National Coordinator for Health Information Technology and/or the U.S. Food and Drug Administration (FDA) is a requirement for all projects. This involves developing a formal Regulatory Pathway Assessment (<https://www.fda.gov/patients/device-development-process/step-3-pathway-approval>) that identifies the regulatory classification and evidentiary requirements for the proposed CDS innovation. This engagement must be formalized through a Q-submission, which is a mandatory milestone for progression to the UH3 phase.

Phase 2 (UH3) - Model Clinical Performance Testing

Following successful transition this phase focuses on gathering compelling evidence of the CDS tool's real-world clinical utility, validating its feasibility for integration into the intended clinical workflows, and demonstrating its positive impact on patient outcomes and/or healthcare processes, thereby catalyzing its clinical adoption.

The total duration of the UG3 and UH3 phases cannot exceed 5 years. This phase may involve prospective studies, including clinical trials if appropriate, to gather evidence on the CDS tool's performance and potential impact in clinical settings.

UH3 Implementation Activities must include, but are not limited to:

- **Data Integration Implementation:** Establish comprehensive and secure data integration processes to effectively combine clinical imaging with essential patient- and cohort-level data streams within clinical workflows prioritizing data security and privacy protection.
- **Multi-site Clinical Validation:** Conduct clinical validation in a targeted healthcare delivery setting (e.g., community hospitals, large academic medical centers) to demonstrate the generalizability of performance across sites for the CDS tool in real-world settings. UH3 plans that propose error detection and mitigation protocols that are reliable across different patient populations and clinical contexts are strongly encouraged, in line with the fundamentals of precision medicine.
- **Continuous Monitoring Framework:** A plan to implement robust methods for ongoing surveillance of model performance and reliability post-deployment, utilizing tools such as AI run charts or equivalent statistical monitoring methods. This framework should align with the FDA's guidance on post-market surveillance, <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/postmarket-surveillance-under-section-522-federal-food-drug-and-cosmetic-act>.

While not required, applicants may propose to conduct clinical trials if appropriate and feasible within the project period. If a trial is proposed, the applicant must thoroughly describe it and provide strong justification for their chosen design. The work supported through an M2C award that includes clinical trial(s) shall be focused on the performance and effectiveness testing of the developed CDS tools in the real-world clinical workflow, and not on trial objectives outside of M2C scope (e.g., costs related to testing a therapeutic).

M2C trials could be either *de novo* dedicated prospective trials or leverage ongoing or planned trials to assess CDS performance as secondary objectives, integrating with existing infrastructure and data streams.

Close collaboration with the PRIMED-AI Validation Center is required throughout Phase 2 (UH3), including:

- **Data and Strategy Sharing:** Comprehensive sharing of relevant data (consistent with approved data sharing plans and IRB protocols) and the detailed sequestration strategy. The scope and parameters of this collaboration must be clearly defined and documented.
- **Standardized Evaluation:** Strict adherence to standardized evaluation protocols established by the Validation Center to ensure consistency and comparability of results, where applicable.
- **Benchmark Utilization:** Systematic use of shared benchmark datasets for comparative analysis and performance benchmarking against established standards, where applicable.
- **Independent Validation:** Regular submission of CDS tools for independent validation by the Validation Center to ensure objective assessment of robustness, fairness, and performance across diverse datasets and clinical scenarios. Independent verification and validation are key activities. Credibility verification is an essential validation activity. Non-regulatory validation activities are necessary during the implementation, distribution, and deployment phase.

Timeline and Milestones

A timeline (Gantt chart) including milestones is required for each phase (UG3/UH3). Milestones are goals that create go/no-go decision points in the project and must include clear and quantitative objective criteria for success. Annual milestones should function as indicators of a project's continued progress, thus revealing emergent difficulties, and will be used to evaluate the application not only in peer review but also in consideration of the awarded project for funding of non-competing award years. Milestones should be well-defined in the application. The following are particularly important:

- Provide appropriately detailed (quantitative) criteria by which milestone achievement will be assessed.
- Provide a detailed timeline for the anticipated attainment of each milestone and the overall goal.
- Identify any impediments that could require an addendum to the research plan, milestones, and/or timeline with a discussion of alternative approaches.

Progression from the UG3 to the UH3 phase is a non-competitive transition contingent upon the successful achievement of all milestones and NIH administrative review. Criteria must be proposed by the applicant(s) and based on quantifiable model performance metrics including, but not limited to:

- **Quantitative Thresholds and Replicability:** PIs must specify the quantitative performance and calibration thresholds (e.g., AUROC, F1-score, clinically relevant utility metric, and/or Expected Calibration Error) that the CDS tool is expected to consistently achieve on clinical imaging, multimodal datasets, and health measures and to ensure reliable probability predictions. These metrics and their corresponding thresholds must meet during independent evaluation by the PRIMED-AI Validation Center on a sequestered retrospective dataset. The plan must also describe how the reproducibility of these metrics will be confirmed during this independent assessment.
- **Regulatory Pathway Alignment:** PIs must outline the specific, tangible outcomes from formal Q-submission to the FDA that will constitute a successful transition milestone. FDA feedback indicating agreement with a proposed regulatory pathway and key evidentiary requirements for market authorization must be documented.

Reporting and Sharing Milestones: The following reports and activities are required for all awardees:

- **Year 1:**
 - Awardees will begin to work with the PRIMED-AI Logistics Center, to establish agreements and policies regarding Intellectual Property (IP) management and data/model sharing with the *Validation Center*.
- **Year 2:**
 - Report from awardees describing the readiness of their algorithms for testing and sharing within the PRIMED-AI ecosystem.
 - Sequestration of data and sharing of models for independent validation by the PRIMED-AI *Validation Center*.
- **Year 3:**
 - Initial submission of CDS tool to the *Validation Center* for iterative, independent testing.
- **Year 5:**
 - Reports from all teams engaged in clinical implementation describing usage of PRIMED-AI tools. Hosting of the PRIMED-AI Final Showcase with contributions from all awardees.
 - Awardees will demonstrate FDA engagement through a pre-submission meeting or formal Q-Submission.

Letters of Support: To highlight the clinical applicability and anticipated dissemination of new technologies and methods, applicants are encouraged to include letter(s) of support from relevant entities. This may include university-based technology transfer office(s), industrial supporters, and collaborators. For all applications, letters of support from healthcare systems or potential industry partners indicating interest in potential licensing, adoption, or collaboration for dissemination upon successful validation are not mandatory but could strengthen the application.

Resource Sharing Plan: Individuals are required to comply with the instructions for the Resource Sharing Plans as provided in the [How to Apply - Application Guide \(https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400\)](https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400).

Other Plan(s):

All instructions in the [How to Apply - Application Guide \(https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400\)](https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400) must be followed, with the following additional instructions:

- A Data Management and Sharing Plan (DMS Plan) is required for any NIH-funded or conducted research that will generate scientific data. Applicants must submit the DMS Plan at the time of application using the [NIH DMS Plan Format Page \(https://grants.nih.gov/grants-process/write-application/forms-directory/data-management-and-sharing-plan-format-page\)](https://grants.nih.gov/grants-process/write-application/forms-directory/data-management-and-sharing-plan-format-page). The DMS Plan must address the elements in the structured format. Where the DMS Plan Format Page requires a "Yes or No" response, no additional narrative is allowed.

Appendix: Only limited Appendix materials are allowed. Follow all instructions for the Appendix as described in the [How to Apply - Application Guide \(https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400\)](https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400).

- No publications or other material, with the exception of blank questionnaires or blank surveys, may be included in the Appendix.

PHS Human Subjects and Clinical Trials Information

When involving human subjects research, clinical research, and/or NIH-defined clinical trials (and when applicable, clinical trials research experience) follow all instructions for the PHS Human Subjects and Clinical Trials Information form in the [How to Apply - Application Guide \(https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400\)](https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400), with the following additional instructions:

If you answered "Yes" to the question "Are Human Subjects Involved?" on the R&R Other Project Information form, you must include at least one human subjects study record using the **Study Record: PHS Human Subjects and Clinical Trials Information** form or **Delayed Onset Study** record.

Study Record: PHS Human Subjects and Clinical Trials Information

All instructions in the [How to Apply - Application Guide \(https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400\)](https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400) must be followed.

Delayed Onset Study

Note: [Delayed onset \(https://grants.nih.gov/grants/glossary.htm#DelayedOnsetStudy\)](https://grants.nih.gov/grants/glossary.htm#DelayedOnsetStudy) does NOT apply to a study that can be described but will not start immediately (i.e., delayed start). All instructions in the [How to Apply- Application Guide \(https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400\)](https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400), must be followed.

PHS Assignment Request Form

All instructions in the How to [Apply- Application Guide \(https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400\)](https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400) must be followed.

Foreign Organizations

Foreign (non-U.S.) organizations must follow policies described in the [NIH Grants Policy Statement \(http://grants.nih.gov/grants/guide/url_redirect.htm?id=11137\)](http://grants.nih.gov/grants/guide/url_redirect.htm?id=11137), and procedures for foreign organizations described throughout the How to Apply- Application Guide.

3. Unique Entity Identifier and System for Award Management (SAM)

See Part 2. Section III.1 for information regarding the requirement for obtaining a unique entity identifier and for completing and maintaining active registrations in System for Award Management (SAM), NATO Commercial and Government Entity (NCAGE) Code (if applicable), eRA Commons, and Grants.gov

4. Submission Dates and Times

Part I. contains information about Key Dates and times. Applicants are encouraged to submit applications before the due date to ensure they have time to make any application corrections that might be necessary for successful submission. When a submission date falls on a weekend or [Federal holiday \(https://grants.nih.gov/grants/guide/url_redirect.html?id=82380\)](https://grants.nih.gov/grants/guide/url_redirect.html?id=82380), the application deadline is automatically extended to the next business day.

Organizations must submit applications to [Grants.gov \(http://grants.nih.gov/grants/guide/url_redirect.htm?id=11128\)](http://grants.nih.gov/grants/guide/url_redirect.htm?id=11128) (the online portal to find and apply for grants across all Federal agencies). Applicants must then complete the submission process by tracking the status of the application in the [eRA Commons \(http://grants.nih.gov/grants/guide/url_redirect.htm?id=11123\)](http://grants.nih.gov/grants/guide/url_redirect.htm?id=11123), NIH's electronic system for grants administration. NIH and Grants.gov systems check the application against many of the application instructions upon submission. Errors must be corrected and a changed/corrected application must be submitted to Grants.gov on or before the application due date and time. If a Changed/Corrected application is submitted after the deadline, the application will be considered late. Applications that miss the due date and time are subjected to the [NIH Grants Policy Statement Section 2.3.9.2 Electronically Submitted Applications \(http://grants.nih.gov/grants/guide/url_redirect.htm?id=82423\)](http://grants.nih.gov/grants/guide/url_redirect.htm?id=82423).

Applicants are responsible for viewing their application before the due date in the eRA Commons to ensure accurate and successful submission.

Information on the submission process and a definition of on-time submission are provided in the [How to Apply-Application Guide \(https://grants.nih.gov/grants-process/write-application/how-to-apply-application-guide\)](https://grants.nih.gov/grants-process/write-application/how-to-apply-application-guide).

5. Intergovernmental Review (E.O. 12372)

This initiative is not subject to [intergovernmental review. \(https://grants.nih.gov/grants/policy/nihgps/html5/section_10/10.10.1_executive_orders.htm\)](https://grants.nih.gov/grants/policy/nihgps/html5/section_10/10.10.1_executive_orders.htm)

6. Funding Restrictions

All NIH awards are subject to the terms and conditions, cost principles, and other considerations described in the [NIH Grants Policy Statement \(http://grants.nih.gov/grants/guide/url_redirect.htm?id=11120\)](http://grants.nih.gov/grants/guide/url_redirect.htm?id=11120).

Pre-award costs are allowable only as described in the [NIH Grants Policy Statement Section 7.9.1 Selected Items of Cost. \(http://grants.nih.gov/grants/guide/url_redirect.htm?id=11143\)](http://grants.nih.gov/grants/guide/url_redirect.htm?id=11143)

7. Other Submission Requirements and Information

Applications must be submitted electronically following the instructions described in the [How to Apply – Application Guide \(https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400\)](https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400). Paper applications will not be accepted.

Applicants must complete all required registrations before the application due date. Section III. Eligibility Information contains information about registration.

For assistance with your electronic application or for more information on the electronic submission process, visit [How to Apply – Application Guide \(https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400\)](https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400). If you encounter a system issue beyond your control that threatens your ability to complete the submission process on-time, you must follow the [Dealing with System Issues \(https://grants.nih.gov/grants/how-to-apply-application-guide/due-dates-and-submission-policies/dealing-with-system-issues.htm\)](https://grants.nih.gov/grants/how-to-apply-application-guide/due-dates-and-submission-policies/dealing-with-system-issues.htm) guidance. For assistance with application submission, contact the Application Submission Contacts in Section VII.

Important reminders:

All PD(s)/PI(s) must include their eRA Commons ID in the Credential field of the Senior/Key Person Profile form. Failure to register in the Commons and to include a valid PD/PI Commons ID in the credential field will prevent the successful submission of an electronic application to NIH. See Section III of this NOFO for information on registration requirements.

The applicant organization must ensure that the unique entity identifier provided on the application is the same identifier used in the organization's profile in the eRA Commons and for the System for Award Management. Additional information may be found in the [How to Apply – Application Guide \(https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400\)](https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400).

See [more tips \(http://grants.nih.gov/grants/guide/url_redirect.htm?id=11146\)](http://grants.nih.gov/grants/guide/url_redirect.htm?id=11146) for avoiding common errors.

Upon receipt, applications will be evaluated for completeness and compliance with application instructions by the Center for Scientific Review and responsiveness by components of participating organizations, NIH. Applications that are incomplete, non-compliant and/or nonresponsive will not be reviewed.

Mandatory Disclosure

Recipients or subrecipients must submit any information related to violations of federal criminal law involving fraud, bribery, or gratuity violations potentially affecting the federal award. See Mandatory Disclosures, [2 CFR 200.113 \(https://www.ecfr.gov/current/title-2/subtitle-A/chapter-II/part-200/subpart-B/section-200.113\)](https://www.ecfr.gov/current/title-2/subtitle-A/chapter-II/part-200/subpart-B/section-200.113) and [NIH Grants Policy Statement Section 4.1.35 \(https://grants.nih.gov/policy-and-compliance/nihgps\)](https://grants.nih.gov/policy-and-compliance/nihgps).

Send written disclosures to the NIH Chief Grants Management Officer listed on the Notice of Award for the IC that funded the award and to the [HHS Office of Inspector Grant Self Disclosure Program \(https://oig.hhs.gov/compliance/self-disclosure-info/hhs-oig-grant-self-disclosure-program/\)](https://oig.hhs.gov/compliance/self-disclosure-info/hhs-oig-grant-self-disclosure-program/) at [grantdisclosures@oig.hhs.gov \(mailto:grantdisclosures@oig.hhs.gov\)](mailto:grantdisclosures@oig.hhs.gov).

Post Submission Materials

Applicants are required to follow the instructions for post-submission materials, as described in [the policy \(http://grants.nih.gov/grants/guide/url_redirect.htm?id=82299\)](http://grants.nih.gov/grants/guide/url_redirect.htm?id=82299)

Any instructions provided here are in addition to the instructions in the policy.

Section V. Application Review Information

1. Criteria

Only the review criteria described below will be considered in the review process. Applications submitted to the NIH in support of the [NIH mission \(http://grants.nih.gov/grants/guide/url_redirect.htm?id=11149\)](http://grants.nih.gov/grants/guide/url_redirect.htm?id=11149) are evaluated for scientific and technical merit through the NIH peer review system.

Overall Impact

Reviewers will provide an overall impact score to reflect their assessment of the likelihood for the project to exert a sustained, powerful influence on the research field(s) involved, in consideration of the following scored review criteria and additional review criteria (as applicable for the project proposed). An application does not need to be strong in all categories to be judged likely to have a major scientific impact.

Scored Review Criteria

Reviewers will consider Factors 1, 2 and 3 in the determination of scientific merit, and in providing an overall impact score. In addition, Factors 1 and 2 will each receive a separate factor score.

Factor 1. Importance of the Research (Significance and Innovation)

Significance

- Evaluate the importance of the proposed research in the context of current scientific challenges and opportunities, either for advancing knowledge within the field, or more broadly. Assess whether the application addresses an important gap in knowledge in the field, would solve a critical problem, or create a valuable conceptual or technical advance.
- Evaluate the rationale for undertaking the study, the rigor of the scientific background for the work (e.g., prior literature and/or preliminary data) and whether the scientific background justifies the proposed study.

Innovation

- Evaluate the extent to which innovation influences the importance of undertaking the proposed research. Note that while technical or conceptual innovation can influence the importance of the proposed research, a project that is not applying novel concepts or approaches may be of critical importance for the field.
- Evaluate whether the proposed work applies novel concepts, methods or technologies or uses existing concepts, methods, technologies in novel ways, to enhance the overall impact of the project.

Specific to this NOFO:

- Evaluate how the proposed integration of diverse data modalities (e.g., imaging, 'omics, clinical, digital sensor data) transcends the limitations of single-modality AI solutions, thereby enabling a fundamentally new level of diagnostic precision, prognostic accuracy, or therapeutic personalization that is currently unattainable.
- Assess to what extent the value proposition for the technically validated CDS tool is clear and compelling to enable precision medicine addressing a highly impactful, unmet clinical need in real-world settings.
- Evaluate the novelty of the clinical image-anchored, multimodal CDS solution based on its impact on an unmet challenge in clinical translation and adoption.

Factor 2. Rigor and Feasibility (Approach)

Approach

- Evaluate the scientific quality of the proposed work. Evaluate the likelihood that compelling, reproducible findings will result (rigor) and assess whether the proposed studies can be done well and within the timeframes proposed (feasibility).

Rigor:

- Evaluate the potential to produce reproducible, robust data.
- Evaluate the rigor of experimental design and whether appropriate controls are in place.
- Evaluate whether the sample size is sufficient and well-justified.
- Assess the quality of the plans for analysis, interpretation, and reporting of results.
- Evaluate whether the investigators presented adequate plans to address relevant biological variables, such as sex or age, in the design, analysis, and reporting.
- For applications involving human subjects or vertebrate animals, also evaluate:
 - the rigor of the intervention or study manipulation (if applicable to the study design).
 - whether outcome variables are justified.
 - whether the results will be generalizable or, in the case of a rare disease/special group, relevant to the particular subgroup.
 - whether the study population appropriately models the target population.
- For applications involving human subjects, including clinical trials, assess the adequacy of inclusion plans as appropriate for the scientific goals of the research. Considerations of appropriateness may include disease/condition/behavior incidence, prevalence, or population burden, population representation, and/or current state of the science.

Feasibility:

- Evaluate whether the proposed approach is sound and achievable, including plans to address problems or new challenges that emerge in the work. For proposed studies in which feasibility may be less certain, evaluate whether the uncertainty is balanced by the potential for major advances.
- For applications involving human subjects, including clinical trials, evaluate the adequacy and feasibility of the plan to recruit and retain a study population that appropriately models the target population. Additionally, evaluate the likelihood of successfully achieving the proposed enrollment based on age, race, ethnicity, and sex.
- For clinical trial applications, evaluate whether the study timeline and milestones are feasible.

Specific to this NOFO:

- Evaluate the scientific rigor of the proposed methods that leverage clinical imaging as the anchor data type with diverse data modalities as the basis of the project. Assess whether the integration strategy accounts for inherent data heterogeneity and varying temporal and spatial resolutions, ensuring the resulting integrated representation is optimal for the intended clinical task.
- Evaluate the specific technical validation metrics and methodologies employed to rigorously assess the contribution and synergistic effect of each integrated modality to the overall performance of the CDS tool. This includes methods to demonstrate that the multimodal approach provides a significant and quantifiable improvement over single-modality or less integrated approaches for the defined clinical problem.
- Assess the logistical and technical feasibility of the proposed pipeline for acquiring, curating, and harmonizing the required clinical-grade multimodal datasets throughout the entire project lifecycle (UG3 and UH3 phases). This includes evaluating the robustness of data access agreements, proposed throughput for data processing, and data governance structures to sustain data quality.
- Evaluate the feasibility of integrating the proposed CDS tool into existing or adaptable clinical workflows. This includes assessing the robustness of proposed implementation strategies, the clarity of anticipated user interaction, and the practical considerations for adoption within multiple clinical sites, as outlined in the "End-User Design/Design for Use in Clinical Care Pathway" section.
- Evaluate the extent to which the plan will promote clinical AI adoption and innovation.

Factor 3. Expertise and Resources (Investigator(s) and Environment)

Investigator(s)

Evaluate whether the investigator(s) have demonstrated background, training, and expertise, as appropriate for their career stage, to conduct the proposed work. For Multiple Principal Investigator (MPI) applications, assess the quality of the leadership plan to facilitate coordination and collaboration.

Environment

Evaluate whether the institutional resources are appropriate to ensure the successful execution of the proposed work.

Additional Review Criteria

As applicable for the project proposed, reviewers will consider the following additional items while determining scientific and technical merit, but will not give criterion scores for these items, and should consider them in providing an overall impact score.

Protections for Human Subjects

For research that involves human subjects but does not involve one of the categories of research that are exempt under 45 CFR Part 46, evaluate the justification for involvement of human subjects and the proposed protections from research risk relating to their participation according to the following five review criteria: 1) risk to subjects; 2) adequacy of protection against risks; 3) potential benefits to the subjects and others; 4) importance of the knowledge to be gained; and 5) data and safety monitoring for clinical trials.

For research that involves human subjects and meets the criteria for one or more of the categories of research that are exempt under 45 CFR Part 46, evaluate: 1) the justification for the exemption; 2) human subjects involvement and characteristics; and 3) sources of materials. For additional information on review of the Human Subjects section, please refer to the [Guidelines for the Review of Human Subjects \(https://grants.nih.gov/grants/guide/url_redirect.htm?id=11175\)](https://grants.nih.gov/grants/guide/url_redirect.htm?id=11175).

Vertebrate Animals

When the proposed research includes Vertebrate Animals, evaluate the involvement of live vertebrate animals according to the following criteria: (1) description of proposed procedures involving animals, including species, strains, ages, sex, and total number to be used; (2) justifications for the use of animals versus alternative models and for the appropriateness of the species proposed; (3) interventions to minimize discomfort, distress, pain and injury; and (4) justification for euthanasia method if NOT consistent with the AVMA Guidelines for the Euthanasia of Animals. For additional information on review of the Vertebrate Animals section, please refer to the [Worksheet for Review of the Vertebrate Animals Section \(http://grants.nih.gov/grants/guide/url_redirect.htm?id=11150\)](http://grants.nih.gov/grants/guide/url_redirect.htm?id=11150).

Biohazards

When the proposed research includes Biohazards, evaluate whether specific materials or procedures that will be used are significantly hazardous to research personnel and/or the environment, and whether adequate protection is proposed.

Resubmissions

As applicable, evaluate the full application as now presented.

Renewals

As applicable, evaluate the progress made in the last funding period.

Revisions

As applicable, evaluate the appropriateness of the proposed expansion of the scope of the project.

Additional Review Considerations

As applicable for the project proposed, reviewers will consider each of the following items, but will not give scores for these items, and should not consider them in providing an overall impact score.

Authentication of Key Biological and/or Chemical Resources

For projects involving key biological and/or chemical resources, evaluate the brief plans proposed for identifying and ensuring the validity of those resources.

Budget and Period of Support

Evaluate whether the budget and the requested period of support are fully justified and reasonable in relation to the proposed research.

2. Review and Selection Process

Applications will be evaluated for scientific and technical merit by (an) appropriate Scientific Review Group(s), convened by CSR, in accordance with [NIH peer review policies and practices \(https://grants.nih.gov/policy-and-compliance/policy-topics/peer-review\)](https://grants.nih.gov/policy-and-compliance/policy-topics/peer-review), using the stated review criteria. Assignment to a Scientific Review Group will be shown in the eRA Commons.

As part of the scientific peer review, all applications will receive a written critique.

Applications may undergo a selection process in which only those applications deemed to have the highest scientific and technical merit (generally the top half of applications under review) will be discussed and assigned an overall impact score.

[Requests for reconsideration of initial peer review \(https://grants.nih.gov/grants/policy/nihgps/html5/section_2/2.4.2_appeals_of_initial_scientific_review.htm\)](https://grants.nih.gov/grants/policy/nihgps/html5/section_2/2.4.2_appeals_of_initial_scientific_review.htm) will not be accepted for applications submitted in response to this NOFO.

Applications will be assigned to the appropriate NIH Institute or Center. Applications will compete for available funds with all other recommended applications submitted in response to this NOFO. Following initial peer review, recommended applications will receive a second level of review by the Council of Councils. The following will be considered in making funding decisions:

- Scientific and technical merit of the proposed project as determined by scientific peer review.
- Availability of funds.
- Relevance of the proposed project to program priorities.

If the application is under consideration for funding, NIH will request "just-in-time" information from the applicant as described in the [NIH Grants Policy Statement Section 2.5.1. Just-in-Time Procedures \(http://grants.nih.gov/grants/guide/uri_redirect.htm?id=82418\)](http://grants.nih.gov/grants/guide/uri_redirect.htm?id=82418). This request is not a Notice of Award nor should it be construed to be an indicator of possible funding.

Prior to making an award, NIH reviews an applicant's federal award history in SAM.gov to ensure sound business practices. An applicant can review and comment on any information in the Responsibility/Qualification records available in SAM.gov. NIH will consider any comments by the applicant in the Responsibility/Qualification records in SAM.gov to ascertain the applicant's integrity, business ethics, and performance record of managing Federal awards per 2 CFR Part 200.206 "Federal awarding agency review of risk posed by applicants." This provision will apply to all NIH grants and cooperative agreements except fellowships.

3. Anticipated Announcement and Award Dates

After the peer review of the application is completed, the PD/PI will be able to access his or her Summary Statement (written critique) via the [eRA Commons \(http://grants.nih.gov/grants/guide/uri_redirect.htm?id=11123\)](http://grants.nih.gov/grants/guide/uri_redirect.htm?id=11123). Refer to Part 1 for dates for peer review, advisory council review, and earliest start date.

Information regarding the disposition of applications is available in the [NIH Grants Policy Statement Section 2.4.4 Disposition of Applications \(http://grants.nih.gov/grants/guide/uri_redirect.htm?id=82416\)](http://grants.nih.gov/grants/guide/uri_redirect.htm?id=82416).

Section VI. Award Administration Information

1. Award Notices

A Notice of Award (NoA) is the official authorizing document notifying the applicant that an award has been made and that funds may be requested from the designated HHS payment system or office. The NoA is signed by the Grants Management Officer and emailed to the recipient's business official.

In accepting the award, the recipient agrees that any activities under the award are subject to all provisions currently in effect or implemented during the period of the award, other Department regulations and policies in effect at the time of the award, and applicable statutory provisions.

Recipients must comply with any funding restrictions described in Section IV.6. Funding Restrictions. Any pre-award costs incurred before receipt of the NoA are at the applicant's own risk. For more information on the Notice of Award, please refer to the [NIH Grants Policy Statement Section 5. The Notice of Award \(https://grants.nih.gov/grants/policy/nihgps/HTML5/section_5/5_the_notice_of_award.htm\)](https://grants.nih.gov/grants/policy/nihgps/HTML5/section_5/5_the_notice_of_award.htm) and NIH Grants & Funding website, see [Award Process. \(https://grants.nih.gov/grants/pre-award-process.htm#award\)](https://grants.nih.gov/grants/pre-award-process.htm#award).

Individual awards are based on the application submitted to, and as approved by, the NIH and are subject to the IC-specific terms and conditions identified in the NoA.

ClinicalTrials.gov: If an award provides for one or more clinical trials. By law (Title VIII, Section 801 of Public Law 110-85), the "responsible party" must register and submit results information for certain "applicable clinical trials" on the ClinicalTrials.gov Protocol Registration and Results System Information Website (<https://register.clinicaltrials.gov> (<https://register.clinicaltrials.gov/>)). NIH expects registration and results reporting of all trials whether required under the law or not. For more information, see <https://grants.nih.gov/policy/clinical-trials/reporting/index.htm> (<https://grants.nih.gov/policy/clinical-trials/reporting/index.htm>).

Institutional Review Board or Independent Ethics Committee Approval: Recipient institutions must ensure that all protocols are reviewed by their IRB or IEC. To help ensure the safety of participants enrolled in NIH-funded studies, the recipient must provide NIH copies of documents related to all major changes in the status of ongoing protocols.

Data and Safety Monitoring Requirements: The NIH policy for data and safety monitoring requires oversight and monitoring of all NIH-conducted or -supported human biomedical and behavioral intervention studies (clinical trials) to ensure the safety of participants and the validity and integrity of the data. Further information concerning these requirements is found at http://grants.nih.gov/grants/policy/hs/data_safety.htm (http://grants.nih.gov/grants/policy/hs/data_safety.htm) and in the application instructions (SF424 (R&R) and PHS 398).

Investigational New Drug or Investigational Device Exemption Requirements: Consistent with federal regulations, clinical research projects involving the use of investigational therapeutics, vaccines, or other medical interventions (including licensed products and devices for a purpose other than that for which they were licensed) in humans under a research protocol must be performed under a Food and Drug Administration (FDA) investigational new drug (IND) or investigational device exemption (IDE).

2. Administrative and National Policy Requirements

The following Federal wide and HHS-specific policy requirements apply to awards funded through NIH:

- The rules listed at [2 CFR Part 200 \(https://www.ecfr.gov/current/title-2/subtitle-A/chapter-II/part-200\)](https://www.ecfr.gov/current/title-2/subtitle-A/chapter-II/part-200), Uniform Administrative Requirements, Cost Principles, and Audit Requirements for Federal Awards.
- All NIH grant and cooperative agreement awards include the [NIH Grants Policy Statement \(http://grants.nih.gov/grants/guide/uri_redirect.htm?id=11120\)](http://grants.nih.gov/grants/guide/uri_redirect.htm?id=11120) as part of the terms and conditions in the Notice of Award (NoA). The NoA includes the requirements of this NOFO. For these terms of award, see the [NIH Grants Policy Statement Part II: Terms and Conditions of NIH Grant Awards, Subpart A: General \(https://grants.nih.gov/grants/policy/nihgps/HTML5/part_ii_terms_and_conditions_of_nih_grant_awards.htm\)](https://grants.nih.gov/grants/policy/nihgps/HTML5/part_ii_terms_and_conditions_of_nih_grant_awards.htm) and [Part II: Terms and Conditions of NIH Grant Awards, Subpart B: Terms and Conditions for Specific Types of Grants, Recipients, and Activities \(http://grants.nih.gov/grants/guide/uri_redirect.htm?id=11159\)](http://grants.nih.gov/grants/guide/uri_redirect.htm?id=11159).

All federal statutes and regulations relevant to federal financial assistance, including those highlighted in [NIH Grants Policy Statement Section 4 Public Policy Requirements, Objectives and Other Appropriation Mandates. \(https://grants.nih.gov/grants/policy/nihgps/HTML5/section_4/4_public_policy_requirements_objectives_and_other_appropriation_mandates.htm\)](https://grants.nih.gov/grants/policy/nihgps/HTML5/section_4/4_public_policy_requirements_objectives_and_other_appropriation_mandates.htm)

By applying for or accepting federal funds from HHS, recipients certify compliance with all federal antidiscrimination laws and these requirements and that complying with those laws is a material condition of receiving federal funding streams. Recipients are responsible for ensuring subrecipients, contractors, and partners also comply.

Applicants and recipients are strongly encouraged to refer to the [NIH Director's Statement of Priorities \(https://www.nih.gov/about-nih/nih-director/statements/advancing-nih-mission-through-unified-strategy\)](https://www.nih.gov/about-nih/nih-director/statements/advancing-nih-mission-through-unified-strategy), entitled "Advancing NIH's Mission Through a Unified Strategy."

Recipients are responsible for ensuring that their activities comply with all applicable federal regulations. Pursuant to 2 CFR 200.340, by accepting an NIH award, the recipient agrees that continued funding for the award is contingent upon the availability of appropriated funds, recipient satisfactory performance, compliance with the Terms and Conditions of the award, and may also otherwise be terminated, to the extent authorized by law, if the agency determines that the award no longer effectuates the program goals or agency priorities, in line with 2 CFR 200.340(a)(4).

Pursuant to the Cybersecurity Act of 2015, Div. N, § 405, Pub. Law 114-113, 6 USC § 1533(d), the HHS Secretary has established a common set of voluntary, consensus-based, and industry-led guidelines, best practices, methodologies, procedures, and processes.

Successful recipients under this NOFO agree that:

When recipients, subrecipients, or third-party entities have:

- ongoing and consistent access to HHS owned or operated information or operational technology systems; and
- receive, maintain, transmit, store, access, exchange, process, or utilize personal identifiable information (PII) or personal health information (PHI) obtained from the awarding HHS agency for the purposes of executing the award.

Cybersecurity plans and procedures **must** at minimum include the following:

- Develop cybersecurity plans and procedures, modeled after the [NIST Cybersecurity framework \(https://www.nist.gov/cyberframework\)](https://www.nist.gov/cyberframework), to protect HHS systems and data:
 - **Identify:**
 - Develop an inventory of all assets and accounts with access to HHS owned and operated information or operational technology systems or which obtain PII or PHI for the purposes of the award.
 - **Protect:**
 - Limit access to HHS owned and operated systems to only those in need of access to complete reward activities.
 - Require all staff to complete annual cybersecurity and privacy awareness training. Visit [405\(d\): Knowledge on Demand \(hhs.gov\) \(https://405d.hhs.gov/kod/five-threats\)](https://405d.hhs.gov/kod/five-threats) to obtain free trainings, if needed.
 - Enable multifactor authentication for all employees, subrecipients, and third-party entities to access HHS owned and operated information or operational technology systems.
 - Regularly backup sensitive data and test backups.
 - **Detect:**
 - Install anti-virus or anti-malware software on all devices, servers, and accounts used to connect to HHS owned and operated systems.
 - **Respond:**
 - Develop an incident response plan. See [Incident-Response-Plan-Basics_508c.pdf \(cisa.gov\) \(https://www.cisa.gov/sites/default/files/publications/Incident-Response-Plan-Basics_508c.pdf\)](https://www.cisa.gov/sites/default/files/publications/Incident-Response-Plan-Basics_508c.pdf) to learn about developing incident response plans.
 - Have cybersecurity incident reporting procedures that ensure the relevant HHS awarding agencies are notified of a cybersecurity incident within 48 hours of discovery. A cybersecurity incident is defined as an unplanned interruption to a technology service or reduction in the quality of a technology service, or an occurrence that actually or potentially jeopardizes the confidentiality, integrity, or availability of an information system or the information the system processes, stores, or transmits.
 - **Recover:**
 - Investigate incidents and plug any security gaps identified.

All activities proposed in your application and budget narrative must align with applicable law, including but not limited to statutes, executive orders, federal regulations and applicable judicial holdings. Accordingly, discretionary awards shall not be used to fund, promote, encourage, subsidize, or facilitate; racial preferences or other forms of racial discrimination by the recipient, including activities where race or intentional proxies for race will be used as a selection criterion for employment or program participation; denial by the recipient of the sex binary in humans, or the belief that sex is a chosen or mutable characteristic; illegal immigration; or any other initiatives that compromise public safety. If an application does not align, the application will not receive funding to the extent permitted by law and applicable court orders.

For applications involving substance abuse, the application must not support harm reduction. Please see [Updated Funding Guidance for Recipients on Supplies and Services \(https://www.samhsa.gov/sites/default/files/dear-colleague-letter-updated-hr-funding-guidance.pdf\)](https://www.samhsa.gov/sites/default/files/dear-colleague-letter-updated-hr-funding-guidance.pdf).

For applications involving funding Medication-Assisted Treatment (MAT) or medications for opioid use disorder (MOUD), this funding should be used to provide comprehensive treatment and recovery support services rather than medication-only models for opioid use disorder. Services should include medications, where clinically indicated, in conjunction with psychosocial and other treatment and recovery support services. Funding can also be used to support individualized tapering and discontinuation of medications when clinically indicated. Please see [Updated Funding Guidance for Recipients on MAT/MOUD \(https://www.samhsa.gov/sites/default/files/dear-colleague-letter-mat-moud-guidance.pdf\)](https://www.samhsa.gov/sites/default/files/dear-colleague-letter-mat-moud-guidance.pdf).

As of October 1, 2025, HHS has adopted 2 CFR Part 200, with some modifications included in 2 CFR Part 300. These regulations replace those in 45 CFR Part 75. However, for NIH, under the Consolidated Appropriations Act for FY 2026, [P.L. 119-75 \(https://gcc02.safelinks.protection.outlook.com/?url=https%3A%2F%2Fwww.congress.gov%2Fbill%2F119th-congress%2Fhouse-bill%2F7148&data=05%7C02%7CantoINETTE.caliman%40nih.gov%7C68a8e1e3db804c61b38f08deb0e88127%7C14b77578977342d58507251ca2dc2b06%7C0%7C0%7C63914270982](https://www.congress.gov/2Fbill/2F119th-congress/2Fhouse-bill/2F7148&data=05%7C02%7CantoINETTE.caliman%40nih.gov%7C68a8e1e3db804c61b38f08deb0e88127%7C14b77578977342d58507251ca2dc2b06%7C0%7C0%7C63914270982) Division B, Title II, Sec. 224), the provisions relating to indirect costs in 45 CFR 75 continue to apply to NIH awards. Consistent with the statute, NIH will not apply updated thresholds outlined within 2 CFR Part 200, at this time.

Cooperative Agreement Terms and Conditions of Award

The following special terms of award are in addition to, and not in lieu of, otherwise applicable U.S. Office of Management and Budget (OMB) administrative guidelines, U.S. Department of Health and Human Services (HHS) grant administration regulations at 2 CFR Part 200, and other HHS, PHS, and NIH grant administration policies.

The administrative and funding instrument used for this Program will be the cooperative agreement, an "assistance" mechanism (rather than an "acquisition" mechanism), in which substantial NIH programmatic involvement with the recipients is anticipated during the performance of the activities. Under the cooperative agreement, the NIH purpose is to support and stimulate the recipients' activities by involvement in and otherwise working jointly with the recipients in a partnership role; it is not to assume direction, prime responsibility, or a dominant role in the activities. Consistent with this concept, the dominant role and prime responsibility resides with the recipients for the project as a whole, although specific tasks and activities may be shared among the recipients and NIH as defined below.

Roles and Responsibilities:

NIH PRIMED-AI Working Group (WG): Consists of NIH programmatic staff from multiple Institutes and Centers of the NIH. This group will be primarily responsible for the stewardship of the PRIMED-AI Program and will participate as non-voting members in the committees.

External Program Consultants (EPCs): External Program Consultants provide critical scientific and managerial insights and recommendations to NIH staff. These recommendations might be relayed to the awardees at the discretion of the NIH. EPC are invited to attend annual meetings and other key events to have awareness of progress and provide feedback to NIH staff in their consulting capacity.

Steering Committee (SC): The SC includes funded contact PIs and NIH PRIMED-AI Program staff to jointly provide scientific input and coordination for the PRIMED-AI Program. It is expected that most of the decisions on the activities of the SC will be reached by consensus. If a vote is needed, each project PD/PI (or Contact PI in the case of multi-PI projects) will have one vote. NIH staff will be non-voting members of the SC. When a vote is required, at least 60% of the votes must be affirmative for approval. To address particular issues, the SC may establish working groups as needed, which will include representatives from the PRIMED-AI Consortium, the NIH, and possibly other experts.

PRIMED-AI Consortium: The PRIMED-AI Consortium will be made up of all PRIMED-AI award recipients. The organizational structure is meant to enable the overall goals of the PRIMED-AI Program.

Project Manager/Director (PM/PD): A dedicated PM/PD responsible for overseeing the entire lifecycle of the project, ensuring it runs smoothly, complies with regulations, and stays on schedule. The PM/PD will be the primary liaison with the PRIMED-AI Logistics Center. This individual should commit at least an appropriate and well-justified level of effort, generally expected to be substantial (e.g., a minimum of 3.0 person-months or 25% FTE, with 50% effort strongly encouraged for complex projects) to the project. The designated PM/PD must have documented experience managing projects of similar scale and complexity, including inter-institutional collaborations. The application must provide evidence of the PM/PD's formal empowerment and clear mandate from all PDs/PIs to oversee project execution, manage timelines, and ensure compliance. A minimum effort of 50% FTE for the PM/PD is strongly recommended for highly complex MPI projects, with detailed justification required if a lower effort is proposed.

The PD(s)/PI(s) will have the primary responsibility for:

- Leading the project as a whole, and agree to accept close assistance, advice, coordination, and collaborate with the NIH PRIMED-AI Program Staff and other award recipients.
- Planning, direction, and execution of the proposed project will be solely that of the PD(s)/PI(s). They will determine experimental approaches, design protocols, set project milestones and conduct experiments.
- Participating in group activities, including the SC to share design and analysis techniques and promote comparability across studies wherever possible.
- Ensuring active participation of partner sites and collaborators in group activities, if applicable.
- Implementing consensus SC recommendations for designing, implementing, evaluating, and disseminating PRIMED-AI Consortium modeling research projects, as appropriate and feasible.
- Agreeing to abide by any policies -- including those regarding intellectual property, data and software release, publication of PRIMED-AI Consortium papers, quality control metrics, standardization, metadata requirements, and public copyright licensing -- that are recommended and consented to by the PRIMED-AI SC and approved by the NIH PRIMED-AI WG, as well as applicable NIH policies, laws, and regulations. Providing information to the NIH Program Official and Project Scientist concerning progress and activities on a regular basis in an agreed upon format, no less than monthly. Attending and participating in SC meetings and accepting and implementing the consensus guidelines and procedures, as appropriate.

Recipients will retain custody of and have primary rights to the data and software developed under these awards, subject to Government rights of access consistent with current HHS, PHS, and NIH policies.

Award recipients must work collaboratively with all members of the PRIMED-AI Consortium to develop and provide usage statistics and quantitative metrics for data and resources for the purposes of programmatic evaluation and continuous improvement. In carrying out stewardship of this NOFO, the PRIMED-AI Program staff may use these metrics to assess effectiveness and communicate the impact of the Program.

NIH Staff has substantial programmatic involvement that is above and beyond the normal stewardship role in awards, as described below:

The Program Official (PO) is a NIH staff member who will provide programmatic oversight and stewardship of the projects, including review of pre-award and award documents/requirements, review of progress reports and budgets, site visits, and any other programmatic issues that may arise. The PO will be responsible for the normal scientific and programmatic stewardship of the award and will be named in the Notice of Award. The PO will make the final determination on the negotiated milestones and will also make the final determination on whether the milestones are met. The PO has the option to recommend, following consultation with the NIH PRIMED-AI Program staff, the withholding or reduction of support from any project that substantially fails to achieve its goals according to the milestones agreed to at the time of the award.

The Project Scientist (PS) is a NIH staff member who will have substantial scientific and programmatic involvement during the conduct of this activity through technical assistance, advice, and coordination. However, the role of NIH staff will be to facilitate and not to direct the activities. It is anticipated that decisions in all activities will be reached by consensus of the PRIMED-AI Consortium and that NIH staff will be given the opportunity to offer input to this process, as a non-voting member.

The NIH PS will have the following substantial involvement:

- Participating with the other SC members in the group process of setting research priorities, deciding optimal research approaches and protocol designs, and contributing to the adjustment of research protocols or approaches as warranted. The PS may facilitate the group process and not direct it.
- Serving as a liaison, helping to coordinate activities among and for the award recipients, including acting as a liaison to the NIH, and as an information resource for the award recipients about other research activities. The PS will coordinate the efforts of the Program with other groups conducting similar studies.
- Attending all SC meetings as a non-voting member and assisting in developing operating guidelines, quality control procedures, and consistent policies for dealing with situations that require coordinated action. The PS will be responsible for working with the PD/PIs in facilitating logistical aspects of the Program.
- Reporting periodically on the progress of the Program to the NIH PRIMED-AI Program staff and leadership.
- Serving as a liaison between the SC and NIH staff.
- Providing oversight and advice in the management and technical performance of the award projects.
- Facilitation of sharing and dissemination of the data and related resources developed in the course of the PRIMED-AI Program to the scientific community at large.

The NIH may enlist additional scientific experts as necessary from within the NIH, or other government agencies, whose function will be to advise the PD(s)/PI(s) in carrying out the goals and aims of the approved studies.

The NIH reserves the right to curtail or phase out the award in the event of (1) a substantial shortfall in accomplishing the management goals and responsibilities as stated in the reviewed application, (2) failure to meet procedures and milestones, and/or (3) substantive changes in the management of award(s) that are not in keeping with the objectives of the NOFO.

Areas of Joint Responsibilities:

Consistent with achieving the goals of the PRIMED-AI Program, the NIH requires all award recipients to collaborate effectively with each other to maximize the chances of overall success of the entire Program. Close interaction among the participating investigators will be required, as well as, significant involvement from the NIH. The award recipients and designated NIH Staff will participate in the annual PRIMED-AI Consortium meeting and scheduled conference calls and share information on data resources, methodologies, analytical tools, as well as preliminary developments. PDs/PIs, key personnel and pre- and post-doctoral trainees are eligible to attend these meetings. EPCs will attend the annual meetings, as well as other relevant NIH staff.

PRIMED-AI Program Evaluation:

Award recipients must work collaboratively with all members of the PRIMED-AI Consortium to develop and provide usage statistics and quantitative metrics for data and resources for the purposes of programmatic evaluation and continuous improvement. In carrying out stewardship of this NOFO, the NIH or its Institutes and Centers may request information essential to an assessment/evaluation of the effectiveness of the PRIMED-AI Program from the award recipients. Award recipients may be contacted during and after the completion of this award for periodic updates on information helpful in evaluating the impact of the program.

Conflict of Interest Management Plan:

The Conflict of Interest Management Strategy for Cooperative Agreements includes several approaches. Decision-making authority on budgetary and funding actions, grants management actions, and management of clinical and regulatory activities and intellectual property issues is assigned to staff of the IC managing the awards. The responsibility for final decision-making may reside with senior NIH management and leadership, separate organizational components and/or oversight committees. It is anticipated that the Project Scientist will refrain from activities that rise to a level of involvement that results in conflicts of interest, for example, co-publication. Should the extent and nature of staff involvement evolve to the level where conflicts of interest arise, NIH will carefully re-evaluate the alignment of duties among Program staff and implement specific strategies to manage the conflicts of interest.

Dispute Resolution:

Any disagreements that may arise in scientific or programmatic matters (within the scope of the award) between award recipients and the NIH may be brought to Dispute Resolution. A Dispute Resolution Panel composed of three members will be convened. It will have three members: a designee of the SC chosen without NIH staff voting, one NIH designee, and a third designee with expertise in the relevant area who is chosen by the other two; in the case of individual disagreement, the first member may be chosen by the recipients. This special dispute resolution procedure does not alter the recipients' right to appeal an adverse action that is otherwise appealable in accordance with PHS regulation 42 CFR Part 50, Subpart D and DHHS regulation 45 CFR Part 16.

3. Data Management and Sharing

A Data Management and Sharing Plan (DMS Plan) is required for any NIH-funded or conducted research that will generate scientific data. Applicants must submit the DMS Plan at the time of application using the [NIH DMS Plan Format Page \(https://grants.nih.gov/grants-process/write-application/forms-directory/data-management-and-sharing-plan-format-page\)](https://grants.nih.gov/grants-process/write-application/forms-directory/data-management-and-sharing-plan-format-page). The DMS Plan must address the elements in the structured format. Where the DMS Plan Format Page requires a "Yes or No" response, no additional narrative is allowed.

Incumbent upon being a Common Fund award recipient, engagement with the [Common Fund Data Ecosystem \(https://commonfund.nih.gov/dataecosystem\)](https://commonfund.nih.gov/dataecosystem) (CFDE) is required for dissemination of PRIMED-AI assets and resources. This may include the sharing of software, CDS tools, AI models, and other related resources with managers of the CFDE infrastructure for the purpose of increasing distribution and integrating with other Common Fund data resources.

Sharing scientific data accelerates biomedical research discovery, in part, by enabling validation and ensuring reproducibility of research results, providing accessibility to high-value datasets, and promoting data reuse for future research studies. PRIMED-AI applicants must provide a Data Management and Sharing Plan. Applicants are encouraged to review the following resources supporting the Data Management and Sharing Plan:

- [Artificial Intelligence in Research: Policy Considerations and Guidance \(https://osp.od.nih.gov/policies/artificial-intelligence/\)](https://osp.od.nih.gov/policies/artificial-intelligence/): <https://osp.od.nih.gov/policies/artificial-intelligence/>
- [NOT-OD-25-081 \(https://www.grants.nih.gov/grants/guide/notice-files/NOT-OD-25-081.html\)](https://www.grants.nih.gov/grants/guide/notice-files/NOT-OD-25-081.html): Protecting Human Genomic Data when Developing Generative Artificial Intelligence Tools and Applications
- Checklist to evaluate the suitability of data for record linkage: https://github.com/NIH-NICHD-Ecosystem/E2_Record-Linkage-Implementation-Checklist/tree/main (https://github.com/NIH-NICHD-Ecosystem/E2_Record-Linkage-Implementation-Checklist/tree/main)

Intellectual Property (IP) Rights

The successful development of multi-modal AI models and the integration of imaging and multimodal data sets on the PRIMED-AI AIP projects are anticipated to require either substantial investment and support by private sector industries, and/or may involve collaborations with other organizations such as academic, other government agencies, and/or non-profit research institutions not directly involved in the PRIMED-AI program. NIH recognizes that intellectual property rights are likely to play an important role in achieving the goals of this program.

To this end, all award recipients shall understand and acknowledge the following:

- The award recipient is solely responsible for the timely acquisition of all appropriate proprietary rights, including intellectual property rights, and all materials needed for the award recipient to perform the project.
- Before, during, and subsequent to the award, the U.S. Government is not required to obtain for the recipient any proprietary rights, including intellectual property rights, or any materials needed by the recipient to perform the project.
- The award recipient is required to report to the U.S. Government all inventions made in the performance of the project, as specified by 35 U.S.C. Sect. 202 (Bayh-Dole Act).
- The award recipient acknowledges the applicability of 35 U.S.C. 200 et. seq. (Bayh-Dole Act) and the resulting US Government rights that apply to any agreements resulting from this NOFO.
- Recipients will have primary rights to the data and resources developed under these awards, subject to Government rights of access consistent with current HHS, PHS, and NIH regulations and policies, including 2 CFR § 200.315.
- The Recipient will declare any relevant Intellectual Property, pre-existing or otherwise, that was not made with the NIH funds, during the application process.

4. Reporting

When multiple years are involved, recipients will be required to submit the [Research Performance Progress Report \(RPPR\) \(http://grants.nih.gov/grants/rppr/index.htm\)](http://grants.nih.gov/grants/rppr/index.htm) annually and financial statements as required in the [NIH Grants Policy Statement Section 8.4.1 Reporting \(https://grants.nih.gov/grants/policy/nihgps/HTML5/section_8/8.4.1_reporting.htm\)](https://grants.nih.gov/grants/policy/nihgps/HTML5/section_8/8.4.1_reporting.htm). To learn more about post-award monitoring and reporting, see the NIH Grants & Funding website, see [Post-Award Monitoring and Reporting \(https://grants.nih.gov/grants/guide/url_redirect.php?id=82428\)](https://grants.nih.gov/grants/guide/url_redirect.php?id=82428).

A final RPPR, invention statement, and the expenditure data portion of the Federal Financial Report are required for closeout of an award, as described in the [NIH Grants Policy Statement Section 8.6 Closeout \(http://grants.nih.gov/grants/guide/url_redirect.htm?id=82420\)](http://grants.nih.gov/grants/guide/url_redirect.htm?id=82420). NIH NOFOs outline intended research goals and objectives. Post award, NIH will review and measure performance based on the details and outcomes that are shared within the RPPR, as described at 2 CFR Part 200.301.

5. Evaluation

Award recipients must work collaboratively with all members of the PRIMED-AI Program to develop and provide usage statistics and quantitative metrics for data and resources for the purposes of programmatic evaluation and continuous improvement. In carrying out stewardship of this NOFO, the PRIMED-AI Program staff may use these metrics to assess effectiveness and communicate the impact of the program.

Section VII. Agency Contacts

We encourage inquiries concerning this funding opportunity and welcome the opportunity to answer questions from potential applicants.

Application Submission Contacts

[eRA Service Desk \(https://www.era.nih.gov/need-help\)](https://www.era.nih.gov/need-help) - Questions regarding ASSIST, eRA Commons, application errors and warnings, documenting system problems that threaten submission by the due date, and post-submission issues.

[Grants.gov Support Center \(https://gcc02.safelinks.protection.outlook.com/?url=https%3A%2F%2Fgrants.gov%2Fsupport&data=05%7C02%7Cantoinette.caliman%40nih.gov%7Caf6dde64d644478d4e8b08dde6700581%7C14b77578977342d58507251ca2dc2b\)](https://gcc02.safelinks.protection.outlook.com/?url=https%3A%2F%2Fgrants.gov%2Fsupport&data=05%7C02%7Cantoinette.caliman%40nih.gov%7Caf6dde64d644478d4e8b08dde6700581%7C14b77578977342d58507251ca2dc2b)
- Questions regarding Grants.gov registration and services (e.g., Workspace, subscriptions).

Scientific/Research Contact(s)

Common Fund PRIMED-AI Program

Email: ODPRIMED-AI@od.nih.gov (<mailto:ODPRIMED-AI@od.nih.gov>)

Peer Review Contact(s)

Center for Scientific Review (CSR)

Email: NOFORReviewContact@csr.nih.gov (<mailto:NOFORReviewContact@csr.nih.gov>)

Financial/Grants Management Contact(s)

Email: NIMHNOFOGrantsManagement@mail.nih.gov (<mailto:NIMHNOFOGrantsManagement@mail.nih.gov>)

Section VIII. Other Information

Recently issued trans-NIH [policy notices \(http://grants.nih.gov/grants/guide/url_redirect.htm?id=11163\)](http://grants.nih.gov/grants/guide/url_redirect.htm?id=11163) may affect your application submission. A full list of policy notices published by NIH is provided in the [NIH Guide for Grants and Contracts \(http://grants.nih.gov/grants/guide/url_redirect.htm?id=11164\)](http://grants.nih.gov/grants/guide/url_redirect.htm?id=11164). All awards are subject to the terms and conditions, cost principles, and other considerations described in the [NIH Grants Policy Statement \(http://grants.nih.gov/grants/guide/url_redirect.htm?id=11120\)](http://grants.nih.gov/grants/guide/url_redirect.htm?id=11120).

Authority and Regulations

Awards are made under the authorization of Sections 301 and 405 of the Public Health Service Act as amended (42 USC 241 and 284) and under Federal Regulations 42 CFR Part 52 and 2 CFR Part 200.